IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

REQUEST FOR FILING
(RULE 53(b)(1))

For Design or Utility Applications

(DO NOT USE FOR CIPs)

Rule 53(b)(1) PATENT APPLICATION:
( ) Continuation)
( ) Divisional) application under 37 CFR 1.53(b)(1)
application under 37 CFR 1.53(b)(1)
of pending prior application of

Group Art Unit: 1621

Examiner: Davis, B.

Inventor(s): MEISEL et al.
Appln. No.: 09 (Series Code ⇧) | 004,926 (Serial No. ⇧)

Atty. Dkt. PM 256868 (New M#) | 97/01 PH/EN (Client Ref)

Filed: January 9, 1998

(Our Deposit Account No. 03-3975
(Our Order No. 11468/256868
C# / New M#

Title: NOVEL MODIFICATIONS OF 2-AMINO-4-(4-FLUOROBENZYLAMINO)-1-ETHOXYCARBONYLAMINOBENZENE, AND PROCESSES FOR THEIR PREPARATION

Date: October 29, 1998

Asst. Commissioner of Patents and Trademarks
Washington, DC 20231

(Parent Matter No. 244517)

Sir:

To effect the above-requested filing today:

1. **Attached** is a copy **(which must be filed)** of the prior application, including:

☒ Abstract
☒ Specification and claims (13 pages) **(must be attached)**
☒ Drawings **(must be attached if originally filed):** 5 sheet(s)/set: ☒ 1 set informal; ☐ Formal of size ☐ A4 ☐ 11"

1A. Always X one box, only:
(1) ☒ Signed declaration or oath as originally filed in prior application attached
(2) ☐ NO declaration or fee is enclosed; therefore, this is a filing under Rule 53(f).

2. ☐ This application is hereby filed by less than all of the inventors named in the prior application. Petition is hereby made requesting deletion as inventor(s) of the following who is/are **not** inventor(s) of the invention being claimed in this application:

1. _____ 2. _____
3. _____ 4. _____
5. _____ 6. _____
7. _____ 8. _____
9. _____ 10. _____

3. The entire disclosure of the prior application is considered as being part of the disclosure of the accompanying application and is hereby incorporated therein by reference thereto.

4. ☒ Priority is claimed under 35 U.S.C. 119/365 based on filing in GERMANY (country) of

	Application No.	Filing Date		Application No.	Filing Date
(1)	19701694.4	20 JAN 1997	(4)		
(2)			(5)		
(3)			(6)		

a. ☐ _____ (No.) Certified copy/copies attached.
b. ☒ Certified copy/copies previously filed on January 9, 1998 in U.S. Application No. 09/004,926 , filed on January 9, 1998.
series code ⇧ ⇧ serial no.
c. ☐ Certified copy/copies filed during International stage of PCT/ ____/____ .

4. (a) ☐ Domestic priority is claimed from PCT/ ____/____ , filed _____ .
(b) ☐ Benefit is claimed of Provisional Application No. 06/_____ , filed _____ .

5. ☒ Prior application is assigned to ASTA MEDICA AKTIENGESELLSCHAFT

by assignment recorded July 9, 1998 (Date) Reel 9308 Frame 0906.

6. ☒ Attached is the following number of Assignments (including original and all later successive ones by different assignors): 1 and respective **new** Cover Sheets. (Do **NOT** file old cover sheets.)

(Assignments in parent **must be refiled** with new Cover Sheets in this continuing application if you want it/them recorded against the continuing application.)

Please return the recorded Assignment to the undersigned.

7. ☒ The power of attorney in the prior application is to Kevin E. Joyce, Reg. No. 20,508
(Name and Reg. No.)
whose current address is as in item 8 below.

a. ☒ Recognize as associate attorney Ann S. Hobbs, Reg. No. 36,830
(Name, Reg. No. and Address)

8. **Address all future communications to Intellectual Property Group of Pillsbury Madison & Sutro LLP, Ninth Floor, East Tower 1100 New York Avenue, N.W., Washington, D.C. 20005-3918**

9. ☒ **Amend the specification** by inserting before the first line the sentence:--This is a ☒ continuation ☐ division of Application No. 09/004,926, filed January 9, 1998
series code ⇧ ⇧ serial no.
.--

9. (a) ☐ **Amend the specification** by inserting before the first line: --This application claims the benefit of Provisional Application No. 60/_____, filed _____ .--

10. ☐ It has been recently determined that this new continuing application is entitled to small entity status. Hence:
___ (No.) Verified Statement(s) establishing "small entity" status under Rules 9 & 27 were/are:
☐ filed in above prior application (and hence applicable hereto)
☐ attached.

11. Petition to extend the life of the above prior application to at least the date hereof
(one box) ☐ is being concurrently filed in that prior application (Use Form PAT-111).
(must be) ☐ was previously filed in that prior application (Check length of prior extension).
(X'd) ☒ is not necessary for copendency (**Double check** before X'ing this box).

12. ☒ **INFORMATION DISCLOSURE STATEMENT:** Attached is Form PTO-1449 listing all of the documents cited by Applicant and the PTO in the parent application(s) relied upon under 35 USC 120 and referenced in item 9 above. Per Rule 98(d) copies of those documents are not required now. Please consider those documents and advise that they have been considered in this new application as by returning a copy of the enclosed Form PTO-1449 with the Examiner's initials in the left column per MPEP 609. .

13. ☐ Attached is a Rule 103(a) Petition to Suspend Action.

14. ☒ **PRELIMINARY AMENDMENT to be entered before fee calculation:** (Do not make amendments here except for correction of improper multiple dependencies or cancellation of whole claims or multiple dependencies for purpose of reducing the filing fee per MPEP §§ 506 and 607; do not cancel all claims).

Please cancel claims 4-14.

FILING FEE

THE FOLLOWING FILING FEE IS BASED ON

->->->->CLAIMS AS FILED AND **CHANGED BY PRELIMINARY AMENDMENT IN ITEM 14**<-<-<-<-

NOTE: If box 1A2 is X'd, do not pay fees, but leave lines 15-22 and 27-32 blank.

				Large/Small Entity		Fee Code
15. Basic Filing Fee .....Design Application				$330/$165		106/26
16. Basic Filing Fee ..... Not Design Application				$790/$395	+790	101/201
17. Total Effective Claims	5	minus 20 =	0	x $22/$11	+0	103/203
18. Independent Claims	5	minus 3 =	2	x $82/$41	+164	102/202
19. If any proper multiple dependent claim (ignore improper) is present,				$270/$135	+0	104/204
20.				**Subtotal =**	**$954**	
21. If "petition" box 13 above is X'd, add petition fee. $130					+0	122
21A. If box 6 above is X'd, add Assignment recording fee ..... $ 40				130	+40	581

22. **TOTAL FILING FEE ATTACHED =** **$994**

(carry forward to Item 31)

23. ☐ ATTACHED:

24. ☐ Preliminary Amendment attached (to be entered after assigning Appln. No.)

25. ☐ The following PRELIMINARY AMENDMENT is to be entered after assigning Appln. No.:

26. **ADDITIONAL FEE CALCULATION FOR PRELIMINARY AMENDMENT PER BOXES 24/25**

	Claims remaining after amendment		Highest number previously paid for		Present Extra			Additional Fee	
						Large/Small Entity			File Code
27. Total Effective Claims	*	minus **	20	=	0	x $22/$11	=	$ 0	(103/203)
28. Independent Claims	*	minus ***	3	=	0	x $82/$41	=	+ 0	(102/202)
29. If amendment enters proper multiple dependent claim(s) into this application for the first time, add (per application) ..... $270/$135								+ 0	(104/204)
30.							ADDITIONAL FEE	$ 0	
31.							plus **FEE** from item 22 on page 3	+ 994	
32.							**TOTAL FEE ATTACHED**	$ 994	

33. *If the entry in this space is less than a entry in the next space, the "Present Extra" result is "0"

34. **If the "Highest number previously paid for" (see item 16 above) is less than 20, write "20" in this space

35. If the "Highest number previously paid for" (see item 17 above) is less than 3, write "3" in this space

CHARGE STATEMENT: Upon the filing of a Declaration pursuant to Rule 60(b) or 60(d), the Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown in the heading hereof for which purpose a duplicate copy of this sheet is attached.
This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed.

Pillsbury Madison & Sutro LLP
Intellectual Property Group

1100 New York Avenue, N.W.
Ninth Floor, East Tower
Washington, D.C. 20005-3918
Tel: (202) 861-3000

By Atty: Ann S. Hobbs **Reg. No.** 36830
Sig: A. S. Hobbs
Fax: (202) 822-0944
Tel: (202) 861-3063

ASH/maf
Atty./Sec.

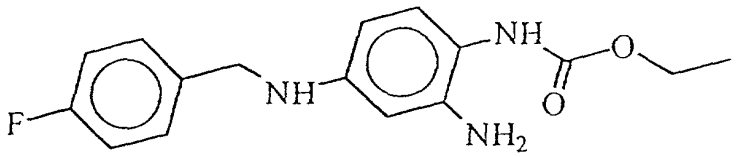
NOTE No. 1: File this Request in duplicate with 2 postcard receipts (PAT-103) & attachments
NOTE No. 2: Is extension in parent necessary for copendency? **DOUBLE CHECK** Item 11 above.

ASTA Medica AG

Novel modifications of 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonylaminobenzene, and processes for their preparation

The invention relates to novel modifications of the compound 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonylaminobenzene of the

formula I



processes for their preparation and their use in pharmaceutical compositions.

The compound of the formula I and it preparation is described in the patent DE 42 00 259.

This compound has, for example, anticonvulsive, antipyretic and analgesic activity and can thus be employed in pharmaceutical preparations.

In the crystallization of the compound of the formula I, however, in some cases very different mixed products are obtained with respect to the crystal size and form. Mixtures of crystal modifications are a great problem for pharmaceutical preparations. In particular, in the case of pharmaceutical forms having a high active compound content, physical inhomogeneties have a disadvantageous effect on adherence to constant pharmaceutical production conditions.

On the other hand, considerable variations in the stability, purity and uniformity of the finished product occur, so that the demands on the pharmaceutical quality of an active compound cannot be satisfied.

It is therefore of great interest to prepare the compound of the formula I in homogeneous crystalline form.

The invention is thus based on the object of preparing the compound of the formula I in homogeneous crystalline form which meets the pharmaceutical requirements.

It has now surprisingly been found that the compound of the formula I can be prepared in 3 different pure crystal modifications. Thus physically homogeneous compounds of the formula I can be prepared for the production of pharmaceutical finished products.

The 3 modifications, called A, B and C, have different physicochemical properties.

The in each case characteristic X-ray diffractograms are used for the identification of these three modifications of the compound of the formula I.

The modifications furthermore differ in their DSC curves (differential scanning calorimetry) and in some cases also in their IR spectra as well as by the crystal forms typical in each case.

The X-ray diffractograms according to Figure 1 were recorded with a powder diffractometer using CuK_α radiation.

The data for the DSC curve according to Figure 2 relate to a heating rate of 10 k/min. The temperatures given

in each case indicate the position of the intensity maximum.

The IR spectra illustrated (Figure 3a, b, c) were recorded on KBr pressed discs.

The modification A is characterized by:

- the X-ray diffractogram, reflections not coinciding with the reflections of the other two modifications being observed, inter alia, at 6.97°2ϑ (12.67 Å), 18.02°2ϑ (4.92 Å) and 19.94°2ϑ (4.45 Å),

- the endothermic A, B conversion effect at approx. 97°C (maximum) below the melting effect of the modification b at approx. 142°C in the DSC curve,

- the IR spectrum differing from the other two modifications by intensive vibration bands at 3421 cm^{-1} (ν N-H) 3376 cm^{-1} (ν N-H), 1703 cm^{-1} (ν C=O) and 886 cm^{-1} (γ C-H), and

- mainly nearly isometric to short-columnar crystals.

The modification B is characterized by:

- the X-ray diffractogram, reflections not coinciding with the reflections of the other two modifications being observed, inter alia, at 15.00°2ϑ (5.90 Å), 19.29°2ϑ (4.60 Å) and 19.58°2ϑ (4.53 Å),

- the absence of thermal effects below the melting effect at approx. 142 °C in the DSC curve and

- mainly longish-tabular to columnar crystals.

The modification C is characterized by:

- the X-ray diffractogram, reflections not coinciding with the reflections of the other two modifications being observed, inter alia, at 9.70°2ϑ (9.11 Å) and 21.74°ϑ [sic] (4.09 Å),

- two endothermic effects connected with the phase transmission to the modification B between approx. 130°C and the melting effect of the modification B at approx. 142°C in the DSC curve and

- mainly tabular crystals.

The preparation of the 3 modifications of the compound I can be carried out by the following processes, adherence to the conditions being of particular importance.

The modifications can be prepared either from the crude product of the compound of the formula I or alternatively by modification conversion.

Preparation of the modification A:

The modification A can be prepared from the modifications B and C by stirring in solvents.

The crystallization of the modification A is preferably carried out with stirring of a supersaturated solution of the compound I in protic, dipolar-aprotic or non-polar solvents.

Protic solvents which can be employed are lower alcohols such as ethanol, 2-propanol, n-butanol, dipolar-aprotic solvents are acetonitrile or acetone and non-polar solvents are [sic] toluene.

The crystallization is preferably carried out in the presence of lower alcohols.

The crystallization from the solution is carried in the temperature range from -20°C to 110°C. In particular, in certain solvents, such as n-butanol, the crystallization of the pure modification A can be carried out at temperatures up to 110°C. The pure modification A is preferably obtained by crystallization in the temperature range from 20°C to 50°C.

<u>Preparation of the modification B:</u>

The crystallization of the modification B is carried out from a saturated solution of the compound I with slow cooling.

The solvents employed can be protic solvents such as water or aprotic solvents such as toluene.

The crystallization is preferably carried out in the presence of toluene.

The crystallization from the solution can be carried out in the temperature range between 50°C to [sic] 110°C, but preferably between 80°C - [sic] 100°C.

The modification B can also be obtained by thermal phase conversion, preferably from the modification A at temperatures of greater than 80°C.

<u>Preparation of the modification C:</u>

The modification C crystallizes out at a temperature of 30°C - 80°C with slow cooling from a saturated solution of the compound I in protic solvents such as ethanol and 2-propanol or aprotic solvents such as toluene.

The crystallization from the solution is preferably carried out at a temperature of 50°C - 70°C.

Each of these modifications of the compound I can be processed for administration in pharmaceutical forms which satisfy the pharmaceutical demands.

The present invention further relates to the use of the modifications A, B and C of the compound I for the production of pharmaceutical preparations. In particular, they are efficacious anti-epileptic agents and neuroprotective agents.

The pharmaceutical preparations can in general contain between 10 mg to [sic] 200 mg of at least one of the modifications of the compound I as an individual dose. Preferred administration forms are tablets.

The modifications of the compound of the formula I can be processed to give the pharmaceutical preparation in a customary manner using suitable exipients and/or auxiliaries.

The modification A of the compound I in particular shows advantageous properties for further pharmaceutical processing.

- The crystal structure is stable up to approx. 80°C. Even after relatively long storage at temperatures up to 60°C and relative atmospheric humidities up to 70%, no lattice changes are observed.

- The modification A undergoes no lattice change on contact with solvents such as, for example, water, ethanol, acetone or toluene.

- The nearly isometric to short-columnar crystal form leads to a grainy substance structure convenient for pharmaceutical processing.

The modifications B and C can be employed for specific pharmaceutical forms such as capsules and dry ampoules. Thus, for example, the preferred formation of finely granular and therefore particularly rapidly soluble crystals observed with the modification C can have advantages for the production of dry ampoules.

The preparation processes for the individual modifications will be illustrated in greater detail with the aid of examples:

<u>Example 1</u>

Modification A

2.34 kg of the compound I and 0.16 kg of active carbon are dissolved by warming with stirring in 7.0 l of ethanol in a 16-l [sic] dissolving vessel. The solution is filtered hot through a pressure filter with stirring into a cooled 32-l [sic] crystallizing vessel with 0.5 l of ethanol such that the internal temperature in the crystallizing vessel is kept at < 45°C. The remaining solution is then rinsed from the dissolving vessel through the pressure filter into the crystallizing vessel using 0.75 l of hot ethanol and the suspension is swiftly cooled. It is subsequently stirred at 5°C - 12°C for 0.5 hours and the solid is filtered off with suction under inert conditions. The product is washed three times with 1.2 l of cooled ethanol each time. The crystallizate is then dried to weight constancy at 50°C - 55°C in a vacuum drying oven. 2.04 kg (87% of theory) of the pure modification A is obtained.

Example 2

Modification A

2 g of the modification C are stirred for 2 days at room temperature in 6 ml of ethanol. The modification A is obtained quantitatively.

Example 3

Modification A

5 g of the modification B or C are stirred for 2 days at room temperature in 50 ml of toluene. The modification A is obtained quantitatively.

Example 4

Modification A

3 g of the modification B are stirred for 2 days at room temperature in 1.5 ml of acetone. The modification A is obtained quantitatively.

Example 5

Modification A

10 g of the compound I are dissolved in 5 ml of n-butanol with warming. The solution is allowed to crystallize at 105°C - 110°C, the mixture is cooled to 20°C and the crystals are washed with n-butanol after filtering off with suction. The modification A is obtained quantitatively.

Example 6

Modification B

10 g of the compound I are briefly heated to reflux with 20 ml of toluene and dissolved. The solution is allowed to crystallize at 90°C - 100°C and the crystals are filtered off with suction and washed with 5 ml of toluene. After drying, 9.8 g (98% of theory) of needle-shaped crystals are obtained.

Example 7

Modification B

10 g of substance of the modification A are kept for 8 hours at 100°C in a drying oven. The modification B is obtained quantitatively.

Example 8

Modification C

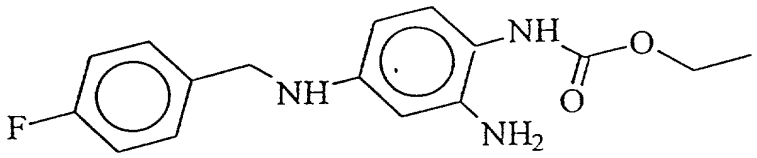
3.0 kg of the compound I are dissolved in a 32-l dissolving vessel by stirring with warming after addition of 0.2 kg of active carbon in 19.6 l of isopropanol. The solution is filtered hot through a pressure filter into a 32-l [sic] crystallizing vessel such that the internal temperature in the crystallizing vessel is kept at 60 - 65°C. The remaining solution is then rinsed from the dissolving vessel through the pressure filter into the crystallizing vessel using 2.5 l of hot isopropanol (about 70°C). After the start of crystallization at 60°C - 65°C, the mixture is subsequently stirred. The suspension formed is swiftly cooled, subsequently stirred at 5°C - 12°C and filtered off with suction under inert conditions. The crystallizate is washed

three times with 2.5 l of cooled isopropanol each time.

The crystallizate is then dried to weight constancy in vacuo at 50°C - 55°C. 2.64 kg (88% of theory) of the active compound are obtained in modification C.

Patent Claims

1. Modification A of the compound I



characterized by the X-ray diffractogram, reflections not coinciding with the reflections of the other two modifications being observed, inter alia, at 6.97°2ϑ (12.67 Å), 18.02°2ϑ (4.92 Å) and 19.94°2ϑ (4.45 Å).

2. Modification B of the compound I characterized by the X-ray diffractogram, reflections not coinciding with the reflections of the other two modifications being observed, inter alia, at 15.00°2ϑ (5.90 Å), 19.29°2ϑ (4.60 Å) and 19.58°2ϑ (4.53 Å).

3. Modification C of the compound I characterized by the X-ray diffractogram, reflections not coinciding with the reflections of the other two modifications being observed, inter alia, at 9.70°2ϑ (9.11 Å) and 21.74°ϑ [sic] (4.09 Å).

4. Process for the preparation of the modification A according to Claim 1, characterized in that the pure crystal form is allowed to crystallize out of a supersaturated solution of the compound I in protic, dipolar-aprotic or non-polar solvents.

5. Process for the preparation of the modification A according to Claim 4, characterized in that the crystallization from the solution is carried out at

temperatures from -20°C to 110°C, preferably at 20°C to 50°C.

6. Process for the preparation of the modification A according to Claims 4 and 5, characterized in that protic solvents which can be employed are lower alcohols such as ethanol, 2-propapanol [sic] or n-butanol, dipolar-aprotic solvents are acetonitrile or acetone and the non-polar solvent is toluene.

7. Process according to Claim 6, characterized in that lower alcohols are preferably used as solvents.

8. Process for the preparation of the modification A according to Claim 1, characterized in that the substance of the modifications B and C are [sic] treated with protic, dipolar-aprotic or non-polar solvents at low temperatures, preferably at room temperature.

9. Process for the preparation of the modification B according to Claim 2, characterized in that the pure crystal form is allowed to crystallize out at a temperature of greater than 80°C from a saturated solution of the compound I in protic or non-polar solvents.

10. Process for the preparation of the modification B according to Claim 9, characterized in that the protic solvent preferably employed is water and the non-polar solvent is toluene.

11. Process for the preparation of modification B according to Claim 2, characterized in that the modification B is preferably prepared from the modification A at temperatures of greater than 80°C by thermal phase conversion.

12. Process for the preparation of the modification C according to Claim 3, characterized in that the pure crystal form is preferably allowed to crystallize out at a temperature of from 50°C to 70°C from a saturated solution of the compound I in protic or alternatively non-polar solvents.

13. Process for the preparation of the modification C according to Claim 12, characterized in

that the protic solvents employed is [sic] preferably ethanol and 2-propanol and the non-polar solvent is toluene.

14. Process for the preparation of the modification C according to Claim 12, characterized in that the crystallization from the solution is preferably carried out at temperatures from 60°C to 70°C.

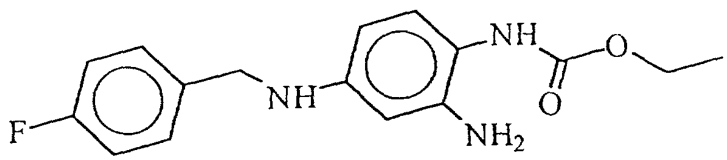
15. Use of the modification A, B and [sic] C of the compound I for the production of pharmaceutical preparations.

16. Pharmaceuticals comprising the modification A, B or C of the compound I and, if appropriate, exipients and/or auxiliaries.

Abstract

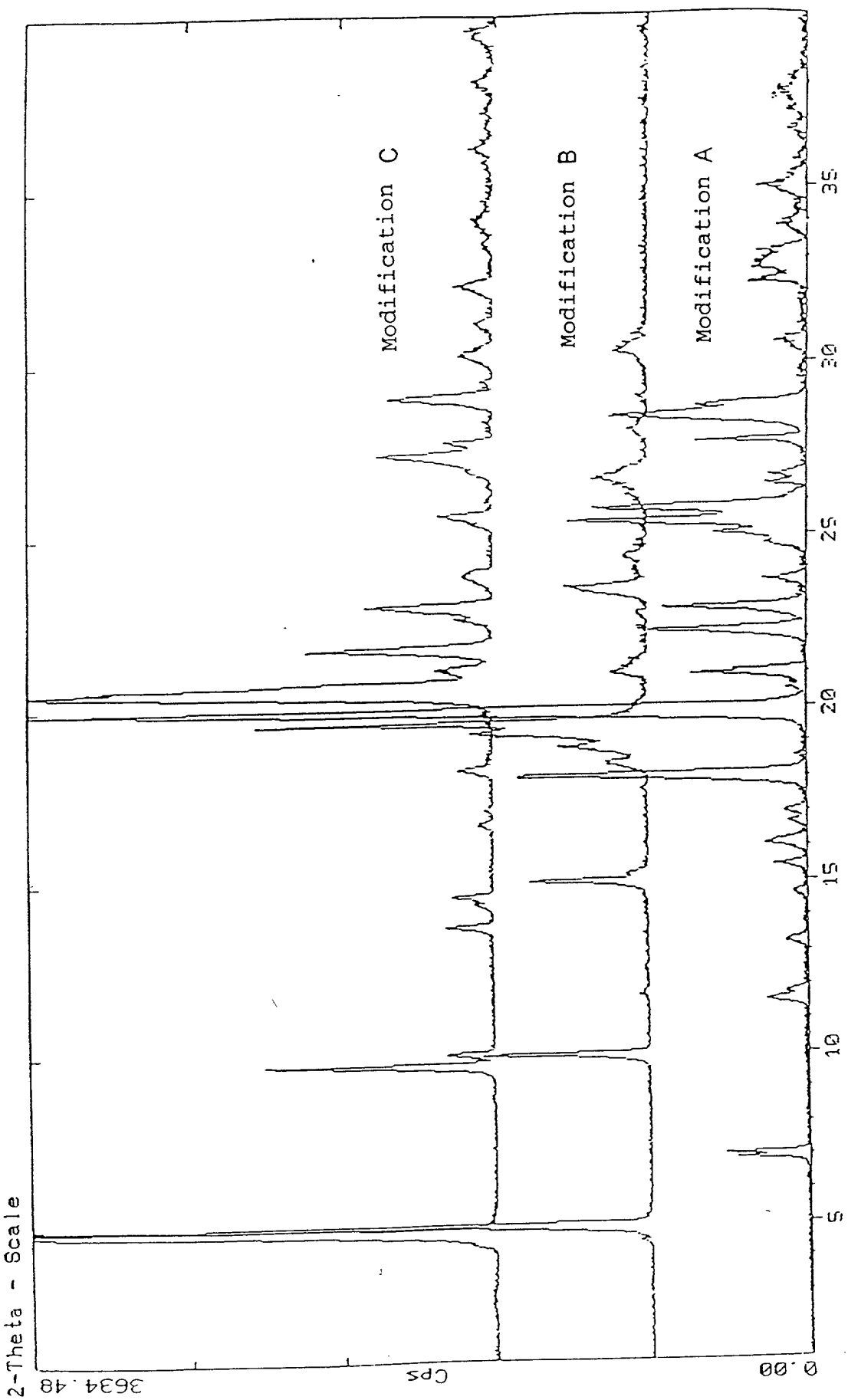
The invention relates to novel modifications of the compound 2-amino-4-(4-fluorobenzylamino)-1-ethoxy-carbonylaminobenzene of the

formula I



processes for their preparation and their use in pharmaceutical compositions.

Figure 1


Modification C
Modification B
Modification A
2-Theta - Scale
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Cps
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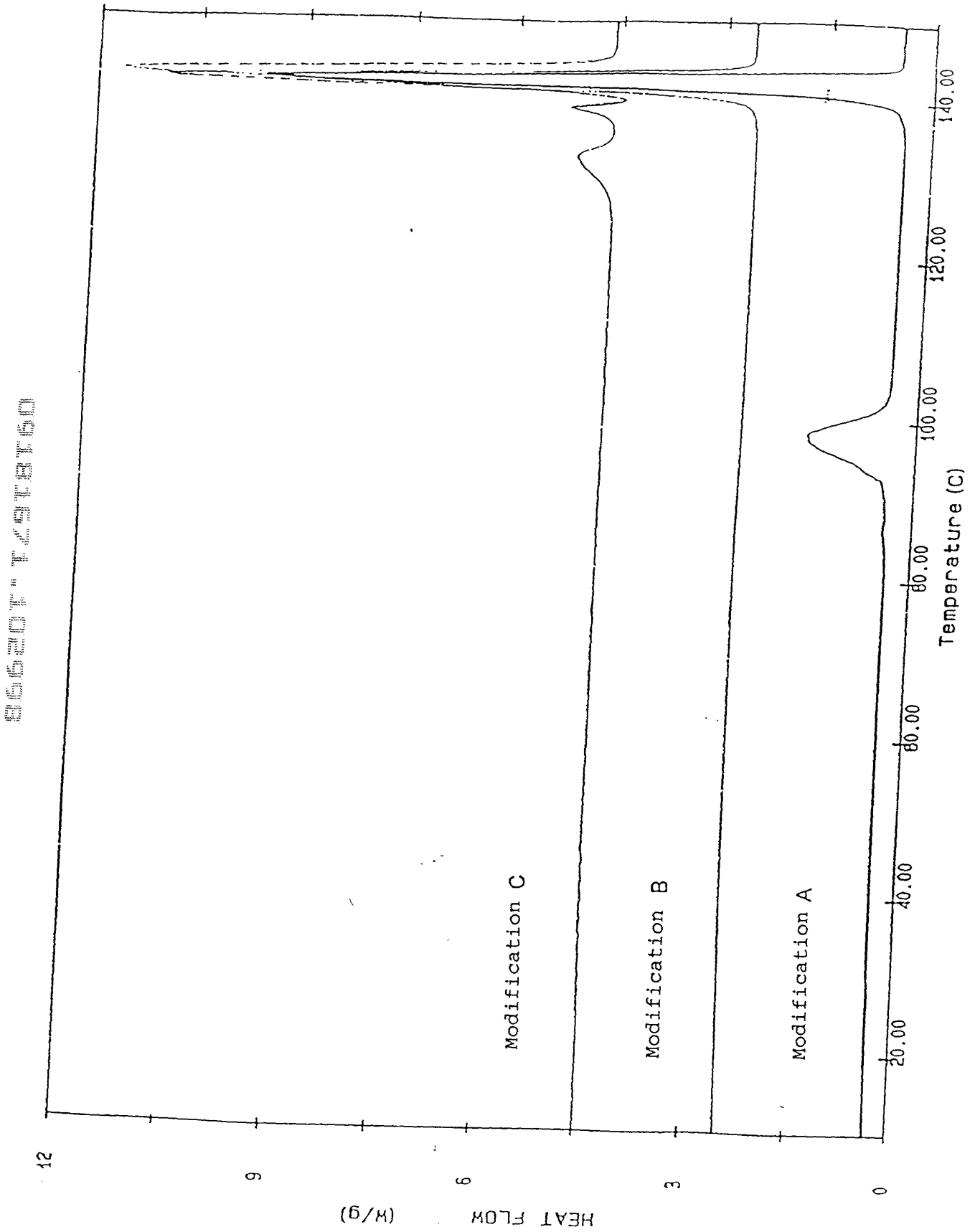
5
10
15
20
25
30
35

Figure 2


Modification C
Modification B
Modification A
HEAT FLOW (W/g)
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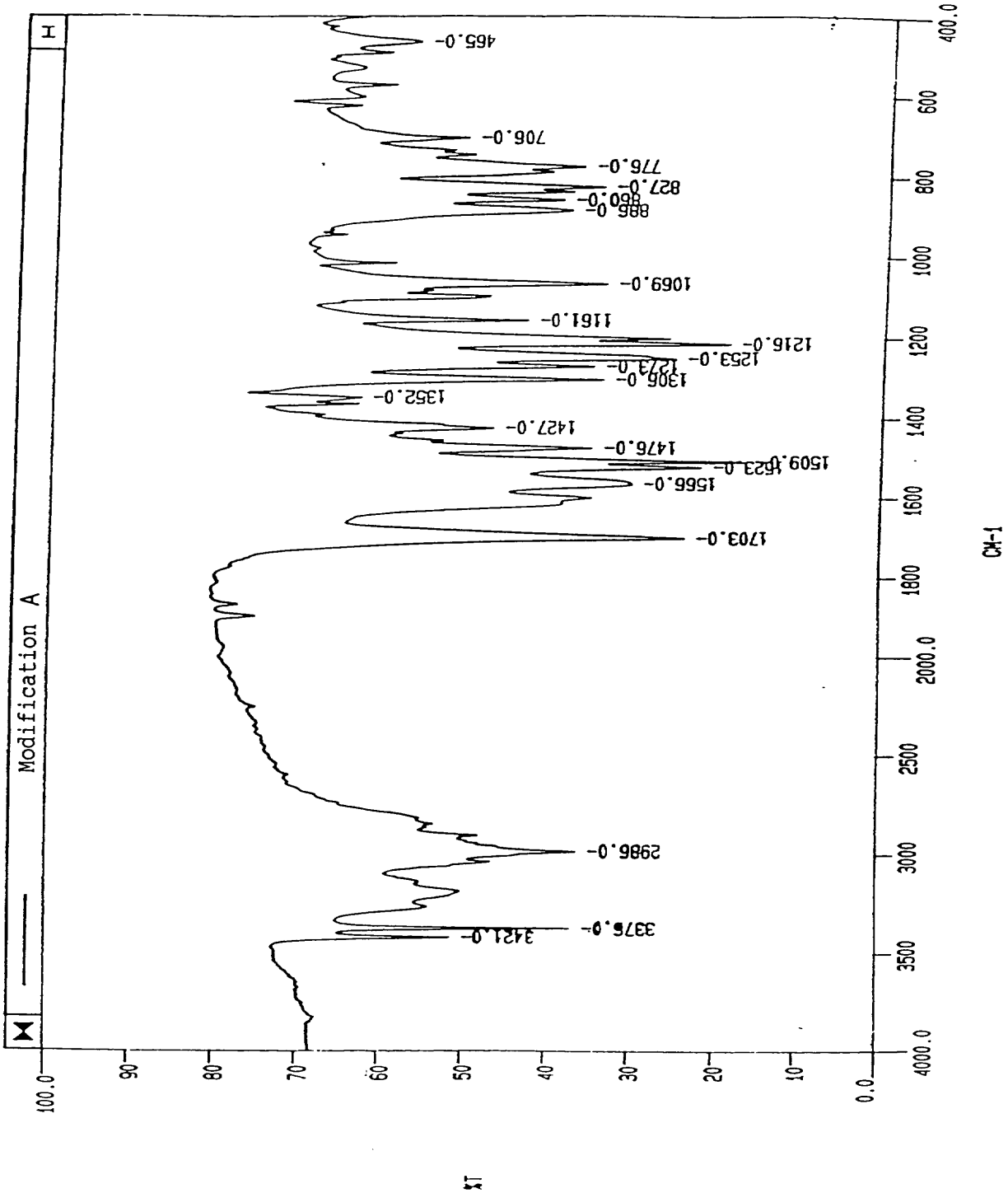
9
6
3
0
20.00
40.00
60.00
80.00
100.00
120.00
140.00
Temperature (C)

Figure 3a


Modification A
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CM-1
100.0
90
80
70
60
50
40
30
20
10
0.0
4000.0
3500
3000
2500
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1800
1600
1400
1200
1000
800
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1352.0
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Figure 3b

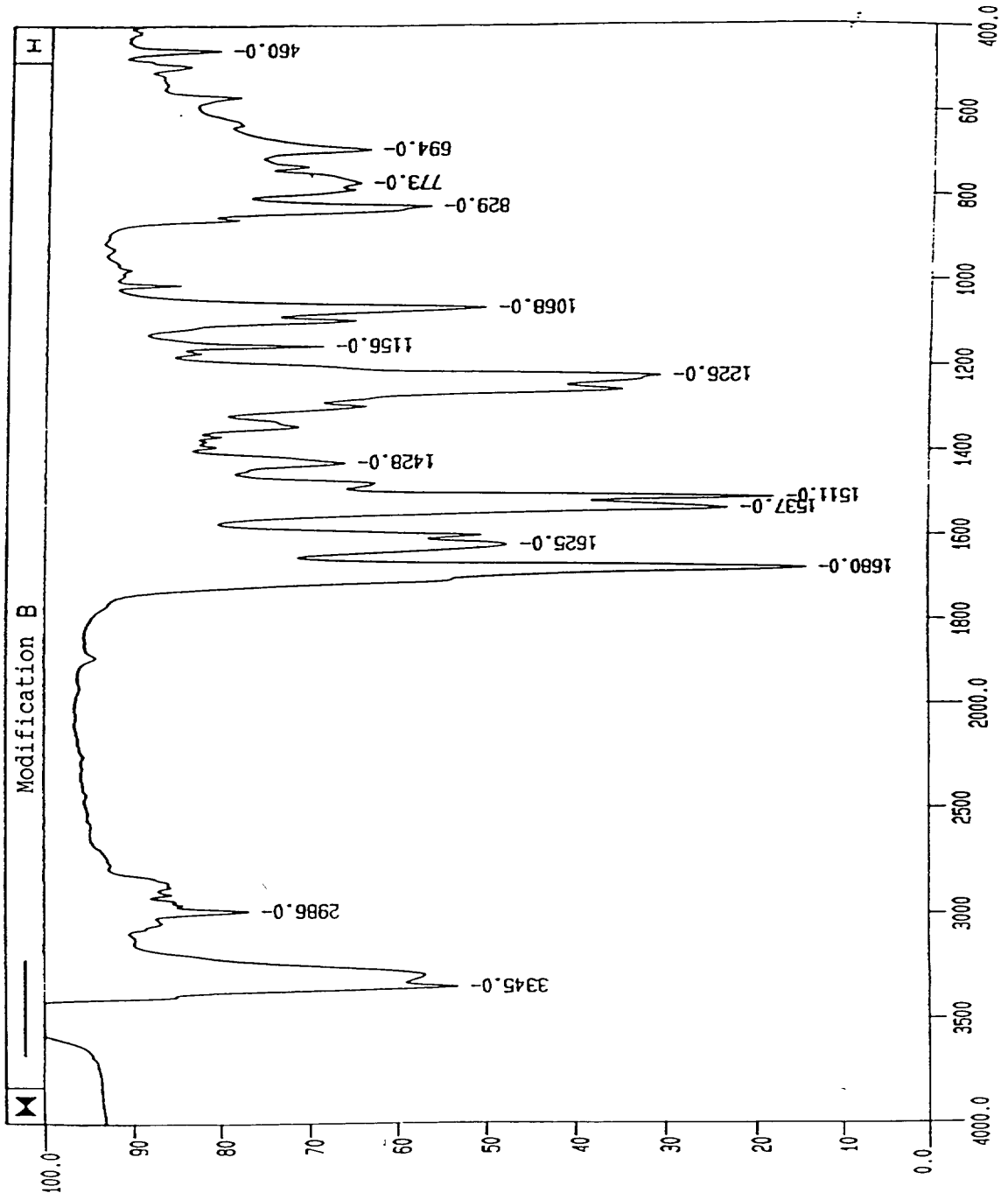
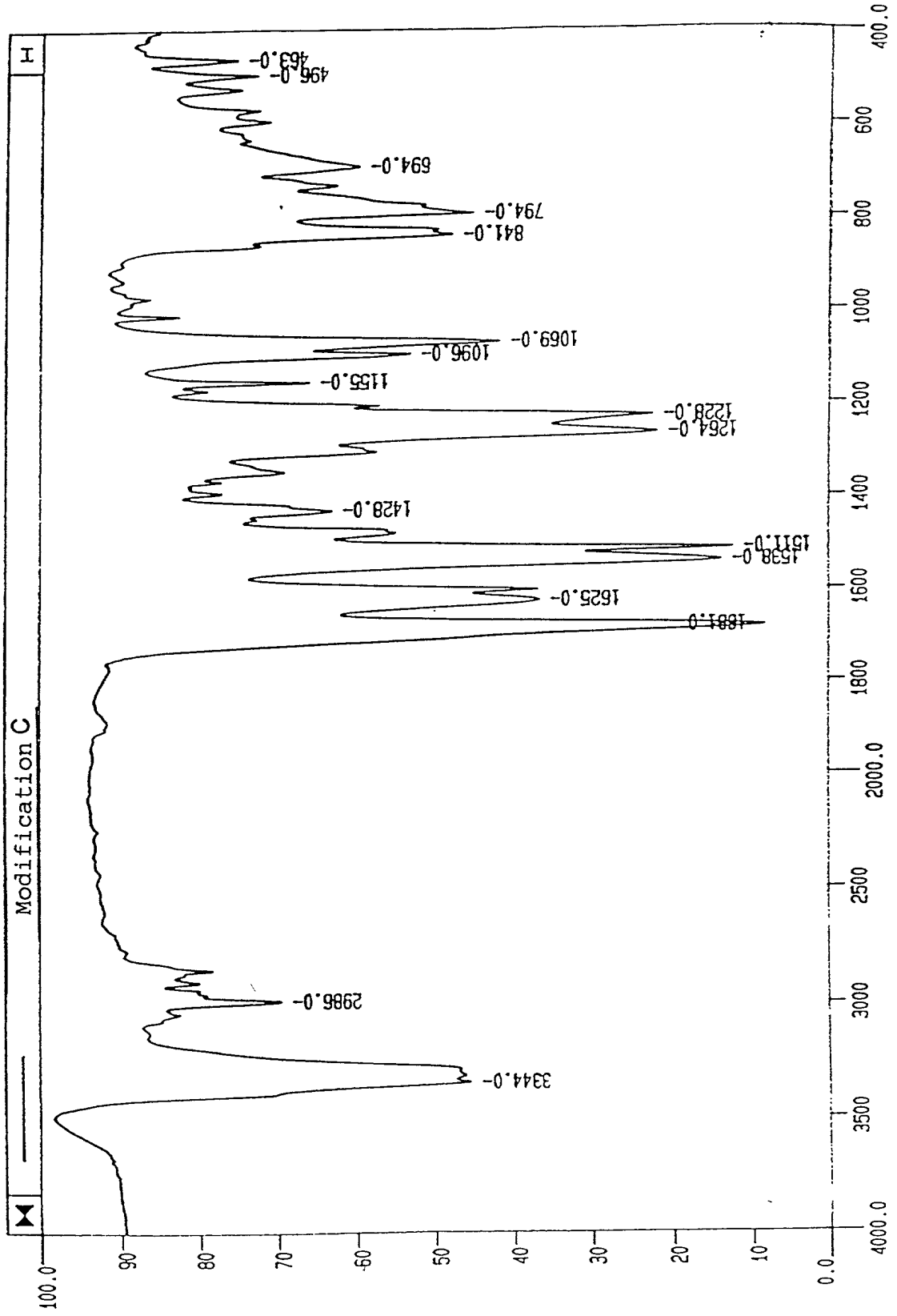


Figure 3c


Modification C
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3000
2500
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1800
1600
1400
1200
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1881.0
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841.0
794.0
694.0
496.0
463.0
CM-1

FOR UTILITY/DESIGN CIP/PCT NATIONAL/PLANT ORIGINAL/SUBSTITUTE/SUPPLEMENTAL DECLARATIONS

RULE 63 (37 C.F.R. 1.63) DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

CUSHMAN FORM

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name, and I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the **INVENTION ENTITLED** NOVEL MODIFICATIONS OF 2-AMINO-4-(4-FLUOROBENZYLAMINO)-1-ETHOXYCARBONYLAMINOBENZENE, AND PROCESSES FOR THEIR PREPARATION

the specification of which (CHECK applicable BOX(ES))

X → ☐ is attached hereto.

BOX(ES) → ☒ was filed on JANUARY 9, 1998 as U.S. Application No. ____/____

→ → ☐ was filed as PCT International Application No. PCT/____/____ on ____

and (if applicable to U.S. or PCT application) was amended on ____

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C.F.R. 1.56. I hereby claim foreign priority benefits under 35 U.S.C. 119/365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate filed by me or my assignee disclosing the subject matter claimed in this application and having a filing date (1) before that of the application on which priority is claimed, or (2) if no priority claimed, before the filing date of this application:

PRIOR FOREIGN APPLICATION(S)			Date first Laid-open or Published	Date Patented or Granted	Priority Claimed	
Number	Country	Day/MONTH/Year Filed			Yes	No
19701694.4	GERMANY	20 JAN 1997			X	

I hereby claim domestic priority benefit under 35 U.S.C. 119/120/365 of the indicated United States applications listed below and PCT international applications listed above or below and, if this is a continuation-in-part (CIP) application, insofar as the subject matter disclosed and claimed in this application is in addition to that disclosed in such prior applications, I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C.F.R. 1.56 which became available between the filing date of each such prior application and the national or PCT international filing date of this application:

PRIOR U.S. PROVISIONAL, NONPROVISIONAL AND/OR PCT APPLICATION(S)		Status	Priority Claimed	
Application No. (series code/serial no.)	Day/MONTH/Year Filed	pending, abandoned, patented	Yes	No

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

And I hereby appoint Pillsbury Madison & Sutro LLP, Intellectual Property Group, 1100 New York Avenue, N.W., Ninth Floor, East Tower, Washington, D.C. 20005-3918, telephone number (202) 861-3000 (to whom all communications are to be directed), and the below-named persons (of the same address) individually and collectively my attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent, and I hereby authorize them to delete names/numbers below of persons no longer with their firm and to act and rely on instructions from and communicate directly with the person/assignee/attorney/firm/ organization who/which first sends/sent this case to them and by whom/which I hereby declare that I have consented after full disclosure to be represented unless/until I instruct the above Firm and/or a below attorney in writing to the contrary.

Paul N. Kokulis	16773	Edward M. Prince	22429	Kendrew H. Colton	30368	Stephen C. Glazier	31361
Raymond F. Lippitt	17519	David W. Brinkman	20817	Michelle N. Lester	32331	Paul F. McQuade	31542
G. Lloyd Knight	17698	Donald J. Bird	25323	Jeffrey A. Simenauer	31993	Ruth N. Morduch	31044
Carl G. Love	18781	W. Warren Taltavull	25647	G. Paul Edgell	24238	Richard H. Zaitlen	27248
Edgar H. Martin	20534	Peter W. Gowdey	25872	Lynn E. Eccleston	35861	Roger R. Wise	31204
William K. West, Jr.	22057	Dale S. Lazar	28872	Timothy J. Klima	34852		
Kevin E. Joyce	20508	Paul E. White, Jr.	32011	David A. Jakopin	32995		
George M. Sirilla	18221	Glenn J. Perry	28458	Mark G. Paulson	30793		

(1) INVENTOR'S SIGNATURE: Peter Meisel Date: 17.2.98

	Peter		MEISEL
	First	Middle Initial	Family Name
Residence	Dresden	Germany	Germany
	City	State/Foreign Country	Country of Citizenship
Post Office Address	Hauptstrasse 32, Dresden, Germany		
(include Zip Code)	01097		

(2) INVENTOR'S SIGNATURE: Karl-Friedrich Landgraf Date: 18.2.98

	Karl-Friedrich		LANDGRAF
	First	Middle Initial	Family Name
Residence	Dresden	Germany	Germany
	City	State/Foreign Country	Country of Citizenship
Post Office Address	Heinrich-Greif-Strasse 37, Dresden, Germany		
(include Zip Code)	01217		

(FOR ADDITIONAL INVENTORS, check box ☒ to attach PAT 116-2 same information for each re signature, *name*, date, citizenship, residence and address.)

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DECLARATION AND POWER OF ATTORNEY
(continued)
ADDITIONAL INVENTORS

(3) INVENTOR'S SIGNATURE: J. Schäfer Date: 25.02.98

First	Middle Initial	Family Name
Jürgen		SCHÄFER

Residence	City	State/Foreign Country	Country of Citizenship
	Radebeul	Germany	Germany

Post Office Address (include Zip Code)	
	Körnerweg 14, Radebeul, Germany 01445

(4) INVENTOR'S SIGNATURE: W. Thiel Date: 18.2.98

First	Middle Initial	Family Name
Wilfried		THIEL

Residence	City	State/Foreign Country	Country of Citizenship
	Langebüuch	Germany	Germany

Post Office Address (include Zip Code)	
	Neulussheimer Str. 26, Langebrüch, Germany 01465

(5) INVENTOR'S SIGNATURE: M. Rischer Date: 2.3.98

First	Middle Initial	Family Name
Matthias		RISCHER

Residence	City	State/Foreign Country	Country of Citizenship
	Maintal	Germany	Germany

Post Office Address (include Zip Code)	
	Thomas-Mann-Strasse 22, Maintal, Germany 63477

(6) INVENTOR'S SIGNATURE: A. Olbrich Date: 6.3.98

First	Middle Initial	Family Name
Alfred		OLBRICH

Residence	City	State/Foreign Country	Country of Citizenship
	Halle/Westf.	Germany	Germany

Post Office Address (include Zip Code)	
	Sauerbruchstrasse 13, Halle/Westf., Germany 33790

(7) INVENTOR'S SIGNATURE: B. Kutscher Date: 27.2.98

First	Middle Initial	Family Name
Bernhard		KUTSCHER

Residence	City	State/Foreign Country	Country of Citizenship
	Maintal	Germany	Germany

Post Office Address (include Zip Code)	
	Stresemannstrasse 9, Maintal, Germany 63477

(8) INVENTOR'S SIGNATURE: Date:

First	Middle Initial	Family Name

Residence	City	State/Foreign Country	Country of Citizenship

Post Office Address (include Zip Code)	

(9) INVENTOR'S SIGNATURE: Date:

First	Middle Initial	Family Name

Residence	City	State/Foreign Country	Country of Citizenship

Post Office Address (include Zip Code)	